REMARKS

Claims

Claims 7 and 9-12 are under examination with claims 8, 13 and 14 withdrawn from consideration due to restriction/election. Claims 1-6 were previously cancelled without prejudice or disclaimer.

Claim 15 is added by this paper.

Claim amendments

Amended claim 7 and 9 are amended as required by the Examiner. Moreover, it is submitted that the subject matter of these claims are directed to the elected invention, for example, a combination comprising the peptide SEQ ID NO: 5 and 8–10. See, original claim 3 and the inclusion thereof in Group XIX of the restriction requirement mailed August 22, 2006.

Claims 8, 13 and 14 have been amended to recite proper dependencies.

Amended claim 11 is drawn to method(s) for making the elected product(s). Entry thereof is respectfully requested.

Support for new claim 15 can be found in, for example, in original claim 6. See also, present claim 10.

It is respectfully submitted that the claim amendments do not raise new matter.

Restriction

The modification in the restriction requirement is noted. It is alleged that based on Applicants' election of Group XIX, claims directed to a combination comprising the peptide of SEQ ID NO: 5 and SEQ ID NOs:8-10, have been elected for examination. Claims 8, 13 and 14 have been withdrawn from consideration. The requirement for restriction is respectfully traversed.

At the outset, Applicants respectfully submit that in view of the forgoing amendments, claim 8, which properly depends on claim 7, be examined on the merits.

The requirement for restriction is improper inasmuch as the Office Action has not demonstrated that an undue searching burden would be required to examine all groups and certainly not to examine at least more than one of the groups. "If search and examination of an entire application can be made without serious burden, the examiner ***must*** examine it on the merits, even though it includes claims to independent or distinct invention." (Emphasis added.) See, M.P.E.P. §803.

Withdrawal of the restriction requirement is earnestly solicited.

Should the Restriction Requirement still be maintained, Applicants will seek reentry of any withdrawn claims once allowable subject matter has been determined. For example, claims 13 and 14 are eligible for rejoinder upon allowance of product claims to which they are dependent on.

Rejection under 35 U.S.C. §112, first paragraph

The contention that claims 7 and 9–12 are non-enabled is respectfully traversed.

The Office Action contends that the instant disclosure does not teach that the peptide having the sequence set forth in SEQ ID NO: 5 is capable of treating hypertension and/or inhibiting ACE. The lack of enablement rejection is further expanded to include peptides of SEQ ID NOs: 8–10 and combinations based thereon. Reconsideration of this rejection is earnestly solicited.

Applicants submit that this contention is misplaced inasmuch as the present specification (for example, the paragraph bridging pages 9 and 10) expressly teaches that "peak No. 4 containing the peptides FPQYLQY (SEQ ID No. 4) and FALPQYLK (SEQ ID No. 5), peak No. 3 containing the peptide FALPQY (SEQ ID No. 3), and peak No. 1 containing the peptide TVY (SEQ ID No. 1) inhibit ACE at more than 70% (emphasis added)." As such, the specification clearly provides an enabling disclosure for the use of the claimed products and/or compositions in a manner recited in the claims. Additionally, since the Office Action fails to provide any evidence on lack of enablement of the claimed products, the contentions of lack of enablement are without legal merit.

The instant specification describes a role of ACE in the etiology of hypertensive disorders. For example, see, the paragraphs bridging page 1 and 2 of the instant specification, as originally filed. It is described therein that ACE has a key role in vivo in regulating arterial pressure and that ACE inhibitors (captoproil, benazepril, enalapril, lisinopril, etc) are one of the main classes of molecules used for combating hypertension. Mechanisms via which ACE regulates atrial pressure, for example, via the rennin-angiotensin system, was appreciated in the field well before the filing date of the instant application. This is clear from the referenced scientific publications by Weber et al. and Piepho et al., the abstracts of which were furnished to the PTO. The Examiner is cordially requested to review the disclosure contained in these scientific abstracts.

It is respectfully submitted that the mere presentation of a rationale for the use of ACE inhibitors having the claimed pharmacological activity (for example, IC_{50} of 60μM or less) and information pertaining to the methods for using such, coupled with a disclosure of the molecules having such activity, is sufficient for enablement. The rationale for the claimed end uses is clearly presented in Applicants' specification. See, for example page 2, lines 6–15 of the originally-filed specification.

The activity of the claimed composition against ACE is also clearly described. Using various biochemical and cellular assays, the specification provides an enabling disclosure of the *in vitro* activity of claimed peptide molecules. See, the paragraph bridging pages 9 and 10 of the specification. A skilled artisan, in view of the detailed disclosure contained in the specification and the art knowledge of pharmacology would appreciate that the claimed molecules and/or compositions can be used in a manner described in Applicants' claims. Nothing more than routine experimentation would be required.

In summary, the specification provides enabling disclosures pertaining to the use of the claimed compositions in the modulation of ACE activity.

Although the specifics of pharmaceutical applications are not required for fulfilling the statutory requirements under §112, ¶1, Applicants' specification nevertheless provides an enabling disclosure for the use of the claimed products in such applications. See, pages 9–11 of the originally-filed specification. Moreover, the enclosed articles by Pan et al. and Li et al. disclose the anti-hypertensive effects of food-derived peptides. The publications clearly establish that the physiological effects of these peptides correlate with the inhibition of the target enzyme, ACE-I. See, for example, Fig. 2 and Fig. 4 of Pan et al. This is consistent with Applicants' claims. Furthermore, Li teaches that structural and functional correlations exist between small molecule ACE inhibitors (such as, for example, captoproil, benazepril, enalapril) and food-derived peptide compounds. See, the paragraphs bridging pages 475-477 of Li et al. Thus, Applicants' own specification, coupled with the knowledge on the structure/activity of both peptide and small-molecule ACE inhibitors, firmly supports enablement of ACE-inhibiting peptide compounds/compositions of the instant invention.

Given the extent of the disclosure provided, it would have at most involved routine experimentation, if any at all, for one skilled in the art to use the claimed molecules as pharmaceutical compositions. For example, see, page 3, lines 11–14. Formulations which confer targeted delivery or desired efficacy are routinely known in the art. Even absent the disclosure as discussed above, the rejection is clearly deficient under general controlling case law. The courts have placed a burden on the PTO to provide evidence shedding doubt on the disclosure that the invention can be made and used as stated. See example *In re Marzocchi*, 439 F.2d 220, 169 USPQ 367 (CCPA 1971). In contrast with the exhaustive disclosure, the present Office Action has not presented any evidence to refute the findings described in Applicants' specification; nor has the Office Action established any scientific credibility to support the contention that the claimed compositions could not be prepared and/or used in a manner described herein. Therefore, the

rejection under 35 U.S.C. §112 is completely unfounded.

The PTO has failed to meet its burden of establishing that the disclosure does not enable one skilled in the art to make and use the compositions recited in the claims. Instead of providing evidence of non-enablement, the Examiner cites the lack of predictability in the field of the hypertension, requiring additional working examples. However, based on the contentions raised in pages 7-8 of the prior Office Action, it appears that the PTO is requiring that the applicant meet the clinical standards as set forth by the FDA to satisfy that enablement requirement under 35 U.S.C. §112, ¶1. This is clearly not the intention of the statute. See, *In re Anthony*, 414 F.2d 1383, 162 USPQ 594 (CCPA 1969). A lack of predictability can be addressed by routine experimentation which is permissible under the statute. A considerable amount of experimentation is permissible if it is merely routine or if the specification in question provides a reasonable amount of guidance with respect to direction which the experimentation should proceed (see *In re Wands* cited by the Examiner). Moreover, as stated in *In re Brana*, 51 F.3d 1516, 34 USPQ 1436 (Fed. Cir. 1995), an Applicant is not required to test the claimed compounds in their final use. The same rationale applies to meeting the enablement and disclosure requirements of 35 U.S.C. §112, first paragraph. The specification provides more than it needs, for example, *in vitro* assays and *in vivo* assays. In similar fashion, one of ordinary skill in the art by performing the same or similar tests can by routine experimentation determine the activity levels of each of the claimed compounds in treating hypertension.

For the reasons discussed above, applicants submit all pending claims satisfy the requirements of 35 U.S.C. §112, first paragraph. Withdrawal of the rejection is respectfully requested.

In view of the above-mentioned arguments and amendments, it is respectfully submitted that the claims in the application are in condition for allowance. However, if the Examiner has any questions or comments, he is cordially invited to telephone the undersigned at the number below.

The Commissioner is hereby authorized to charge any fees associated with this response to Deposit Account No. 13-3402.

Respectfully submitted,

/Anthony J. Zelano/
Anthony J. Zelano, Reg. No. 27,969
Attorney for Applicant(s)

MILLEN, WHITE, ZELANO
& BRANIGAN, P.C.
Arlington Courthouse Plaza 1, Suite 1400
2200 Clarendon Boulevard
Arlington, Virginia 22201
Telephone: (703) 243-6333
Facsimile: (703) 243-6410

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